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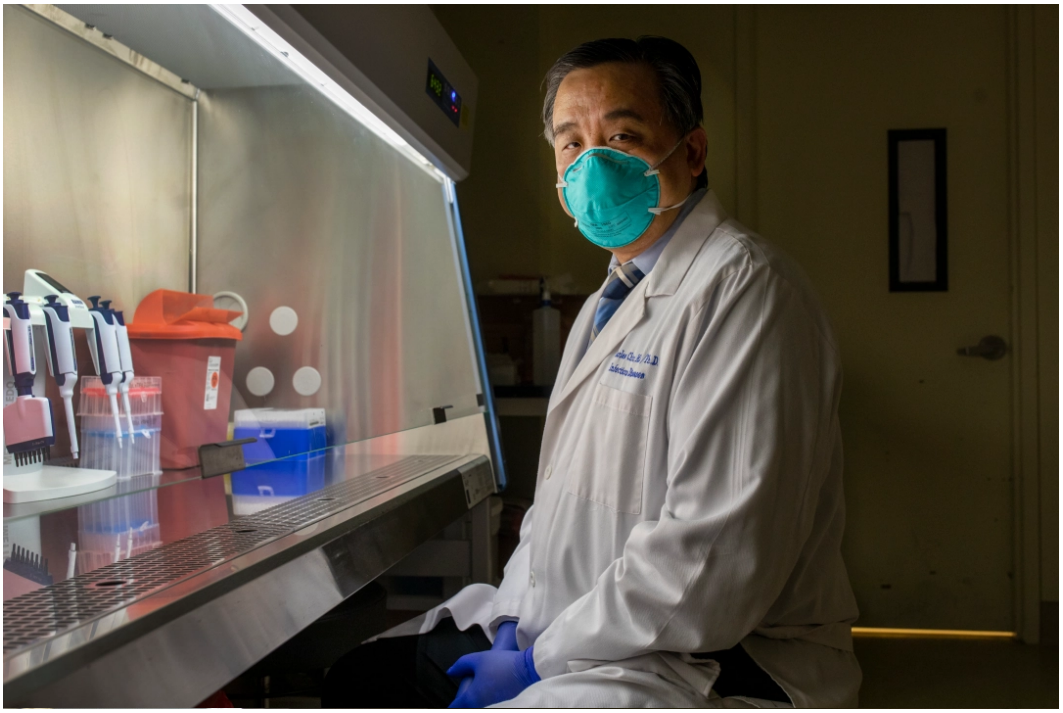
New UCSF study: Vaccine-resistant viruses are driving 'breakthrough' COVID infections

'As long as the virus continues to circulate, it will continue to mutate'



SAN FRANCISCO, CA. – DEC. 30: Dr. Charles Chiu of UCSF is sequencing hundreds of Northern California viruses from recent UK travelers to help understand the latest mutations. He was photographed Wednesday, Dec. 30, 2020, in San Francisco, Calif. (Karl Mondon/Bay Area News Group)

By **LISA M. KRIEGER** | lkrieger@bayareanewsgroup.com | Bay Area News Group

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Waning immunity and ferocious contagion are known to be fueling the troubling surge in "breakthrough" COVID-19 cases among vaccinated people.

But a new UC San Francisco analysis of 1,373 Bay Area cases reveals a third, and more ominous, problem: The coronavirus is learning to outsmart our immune system.

Variants with antibody-resistant mutations are playing an ever-larger role in our highly vaccinated region's pandemic, according to research by prominent virologist Dr. Charles Chiu.

His team found that 78% of infections in fully vaccinated people among the study were caused by variants with these mutations, compared to 48% of the cases among unvaccinated people, who remained an easier target for earlier generations of the virus. Overall, the proportion of cases linked to these variants more than doubled between February and June.

The findings add to a growing list of studies that are unraveling why the vaccinated are still so susceptible to infection — and provide a deeper understanding of what we may encounter in the future.

Vaccinated people are still much more protected from serious illness, hospitalization and death than unvaccinated people, the study confirmed.

"But I worry that as long as the virus is circulating, it will continue to mutate and evolve, which will, in turn, allow it to continue spreading," he said.

The study suggests that new iterations of the virus will likely become even more resistant, over time, "until, eventually, you're going to see the vaccine not work, or its efficacy will be reduced significantly," he said.

Our vaccines won't suddenly become useless, he added. So far, it appears to be a gradual process. The resistant variants will slowly dominate over time, he predicted.

The rollout of booster vaccines, planned to begin the week of Sept. 20, will help bolster our defense against these breakthroughs, Chiu said.

But as the virus continues to evolve, he said, vaccines may need to be reformulated to keep us safe.

The team's second major finding was more reassuring: People who never develop symptoms during a "breakthrough" infection carry very low levels of virus – a finding that should ease concerns that vaccinated people are unknowingly fueling the pandemic.

However, vaccinated people who do have symptoms had the same levels of virus as infected unvaccinated people – so can spread the virus. This confirms a finding first revealed weeks ago by a CDC study in Provincetown, Massachusetts.

"You're essentially as infectious as someone who was unvaccinated," he said.

The UCSF team performed genome sequencing of viral samples from Bay Area residents who sought treatment for COVID-19 at UCSF hospitals and clinics between Feb. 1 and June 30, as well as people whose infections were detected at community test sites. Of these, 125, or 9.1%, were vaccine "breakthrough" cases. The study, published as a preprint on Wednesday, has not yet been peer-reviewed or corroborated by other investigators.

A great concern is the study's observation that vaccinated people infected with these "escape mutants" can likely transmit them to others, including the vaccinated, said infectious disease expert Dr. Gary Schoolnik, a clinician and professor of medicine at Stanford Health Care, who was not involved in the study.

"The implication of their finding is that vaccine-resistant mutants of the COVID virus could disseminate more widely in the population," he said. "If that were to occur, it might necessitate the development and use of COVID booster vaccines that specifically target such mutants."

Overall, three factors are driving breakthroughs, according to Chiu, director of the UCSF-Abbott Viral Diagnostics and Discovery Center and associate director of the UCSF Clinical Microbiology Laboratory.

One is exposure to the large number of viral particles shed by those infected with the delta variant. People infected with delta may shed approximately four times more virus than those infected with the original virus. A few of these viruses can slip by our antibody defense, causing infection.

Another is waning immunity, according to recent Moderna and Pfizer vaccine data. Six to nine months after vaccination, our bodies produce fewer effective antibodies.

The third reason is this newer and worrisome trend: infection by a variant carrying resilient mutations. The new study found that the proportion of cases caused by these variants increased over five months from 40% to 89%.

The team did not study the effect of the mutations on the effectiveness of the other arm of the immune system, involving T cells that kill the virus.

Vaccination is not to be blamed for the increase in variants with these mutations, Chiu said. Because we naturally produce antibodies in response to exposure and infection, the virus is constantly changing to survive.

"The virus is going to evolve to become antibody resistant, whether or not you deploy a vaccine," he said. "But because we have a vaccine, there's a way to prevent the virus from spreading and evolving further."

One of these mutations, L452R, is built into the genetic code of the dangerous delta variant, which now dominates. But this and other mutations, including E484K and F490S, can be carried by other resistant variants, such as beta, gamma, epsilon and lambda. Our antibodies are less effective in fighting off variants carrying these mutations.

These mutations don't render our antibodies useless against the virus. Resistance is almost always partial; it's not an "all or none" characteristic.

"This decrease in vaccine efficacy due to infection by a resistant variant can be minor, or significant," he said.

The mutations make it tougher for antibodies to bind to the virus, so the virus is able to slip through and infect a cell. More of them are needed to neutralize the virus.

A booster dramatically increases our levels of antibodies. A new and reformulated booster, targeted for a particular variant such as delta, could push them still higher.

Ultimately, we will control this pandemic by vaccinating as many people as possible, Chiu said.

"Otherwise, if the virus continues to circulate and mutate," he said, "this may become a never-ending round of whack-a-mole."

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Lisa M. Krieger is a science writer at The Mercury News, covering research, scientific policy and environmental news from Stanford University, the University of California, NASA-Ames, U.S. Geological Survey and other Bay Area-based research facilities. She graduated from Duke University with a B.A. degree in biology. She splits her time between Palo Alto and Inverness, and in her spare time likes wildlife photography, swimming, skiing and backpacking.

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